

Autoimmune/ Idiopathic Neutropenia

National Neutropenia Network Meeting
Cincinnati, OH

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Outline

- Autoimmune Neutropenia
- Idiopathic Neutropenia
- Supportive care:
 - Oral Care
 - Bone Health

Neutropenia

Severity of Neutropenia	Absolute Neutrophil Count (ANC)
Mild	Between 1000-1500/uL
Moderate	Between 500-1000/uL
Severe	<500/uL

Neutropenia



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graph TD; A[Neutropenia] --> B[Congenital]; A --> C[Acquired]; C --> D[Autoimmune]; C --> E[Idiopathic]; C --> F[Drugs/toxins]; C --> G[Infection]; C --> H[Malignancy]; C --> I[Nutrition];
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The diagram is a flowchart starting with 'Neutropenia' in a dark blue box at the top. A line connects it to two boxes below: 'Congenital' in a green box on the left and 'Acquired' in a light blue box on the right. From the 'Acquired' box, a line leads down to a larger light blue box containing a list of causes: 'Autoimmune' (highlighted with a red border), 'Idiopathic', 'Drugs/toxins', 'Infection', 'Malignancy', and 'Nutrition'.

Congenital

Acquired

Autoimmune

Idiopathic

Drugs/toxins

Infection

Malignancy

Nutrition

Autoimmune Neutropenia (AIN)

- Low neutrophil count resulting from increased peripheral destruction due to antibodies targeting the cell membrane antigens

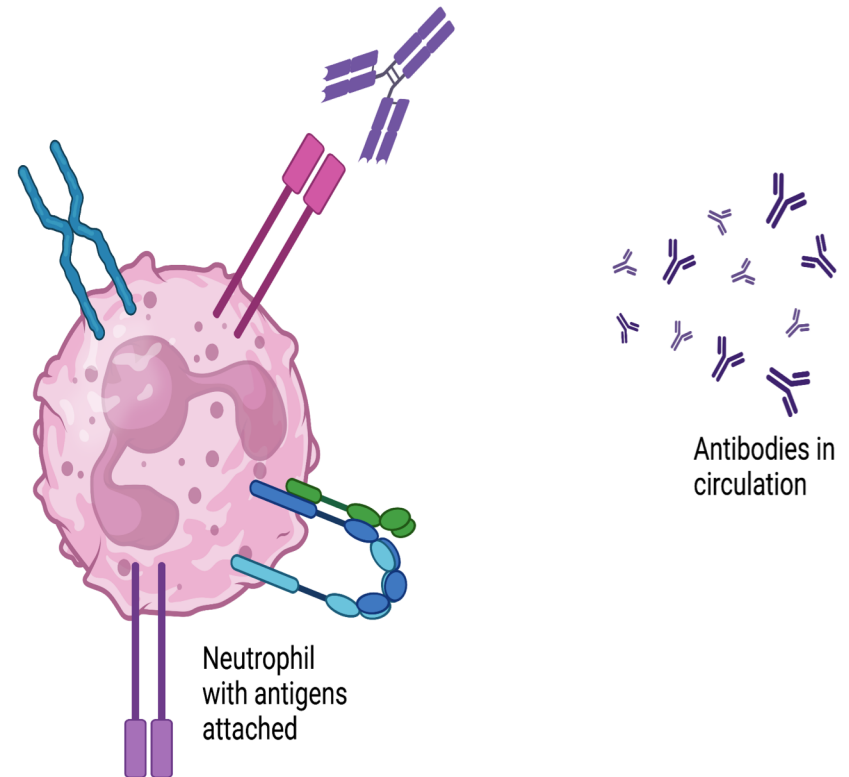


Image created on Biorender

Primary vs Secondary AIN

- **Primary Autoimmune Neutropenia:** not associated with other conditions
- **Secondary Autoimmune Neutropenia:** Usually due to underlying conditions eg. autoimmune/rheumatological or hematological processes

Primary AIN

- Diagnosed around ~4-6 months of life to 4 years of age
- Significant neutropenia 500-1000/uL at diagnosis
- The majority of patients will experience a spontaneous remission where blood counts will normalize by 3-5 years of age
- Adults may develop a chronic form

Clinical Course

- Course is usually **benign** but with the potential for infectious complications based on the degree of the neutropenia:
 - Pneumonia
 - Sepsis
 - Meningitis
 - Ear infections
 - Cellulitis

Autoantibodies

- **Antibodies responsible for primary AIN act against Human Neutrophil Antigen (HNA)**
 - These antigens express proteins, which attached to the plasma membrane of neutrophils

Human neutrophil antigen nomenclature

Majority of cases involve HNA1a and 1b

Antigen system	Antigen	Glycoprotein	Acronym
HNA-1	HNA-1a	FcγRIIIb	NA1
	HNA-1b	FcγRIIIb	NA2
	HNA-1c	FcγRIIIb	SH
HNA-2	HNA-2a	gp50–64	NB1
HNA-3	HNA-3a	gp70–95	5b
HNA-4	HNA-4a	CD11b	MART
HNA-5	HNA-5a	CD11a	OND

Capsoni et. al, 2005

Where do the antibodies come from?

- Molecular mimicry when the body is exposed to infections
- Drug exposure
- Loss of suppressor activity against self reactive lymphocyte

Treatments

- Primary AIN are usually self limiting and require **no specific treatment**

Infection history:

- Antibiotic prophylaxis can be assessed case by case
- Intravenous Immunoglobulins (IgG)
- Granulocyte colony stimulating factor (GCSF) in certain cases

GCSF

- Goal neutrophil count $> 1000/\mu\text{L}$
- Stimulate proliferation and maturation of neutrophil progenitors
- Release mature cells into the bloodstream
- Stimulates phagocyte function
- Reduces the neutrophil breakdown
- Raises levels of the soluble FcReceptor for antibodies to bind

Secondary AIN

- Most present in adulthood but can affect all age ranges
- Women > Men
- **Less likely to resolve** as they are often attributed to:
 - Systemic autoimmune disease e.g. Sjogren's syndrome, SLE, Rheumatoid Arthritis
 - Infection
 - Cancers, stem cell transplant or solid organ transplant
 - Medications
 - Infections- viral/ bacterial triggers

Diagnosis of AIN

- Anti-neutrophil antibodies may be detectable in the blood but **absence** of a positive test to these antibodies **does not** rule it out
- **A positive test does not rule out congenital neutropenia**
- Repeat negative tests, development of other abnormalities in blood counts or other immune dysregulation, consider other diagnoses and a bone marrow aspirate

Neutropenia



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```

A flowchart illustrating the classification of Neutropenia. The root node is 'Neutropenia' in a dark blue box. It branches into 'Congenital' (green box) and 'Acquired' (light blue box). The 'Acquired' box further branches into a list of causes: 'Autoimmune', 'Idiopathic' (highlighted with a red border), 'Drugs/toxins', 'Infection', 'Malignancy', and 'Nutrition'.

Congenital

Acquired

Autoimmune

Idiopathic

Drugs/toxins

Infection

Malignancy

Nutrition

Idiopathic Neutropenia

- Chronic Idiopathic Neutropenia (CIN):
ANC < 1500/ uL on at least 3 occasions
for more than 3 months in the absence or
presence (if the adult form) of antibodies
- Diagnosis of **exclusion**
 - **Must rule out congenital and other
secondary forms of neutropenia**

Clinical Course

- Frequency and severity of infections will relate to the degree of neutropenia
- Most patients will respond to GCSF

Supportive care

Dental Care

- Oral Manifestations:
 - Canker sores or aphthous ulcers
 - Gingival hypertrophy or gingivitis
 - Periodontal disease

Fig. 1 Enlargement of buccal gingival tissue associated with maxillary anterior teeth of our patient



Hajishengallis et. al, 2016

Recommendations:

- Encourage good mouth care including flossing and regular dental checkups
- Plaque control
- Mouthwashes like chlorhexidine (Peridex) may be beneficial
- May consider GCSF
- Antimicrobial rinses or antibiotics in the case of infections

Bone Health

- Low bone mineral density (BMD) is a risk factor for fractures
- Low BMD has been reported in patients with severe chronic neutropenia
- Study from SCNIR, total of 128 subjects (adult and pediatrics)
 - n=57 Idiopathic neutropenia
 - n= 3 Autoimmune
- 17.5% of children had BMD scores that were low for age
- 46% of adults had osteopenia and 9% met osteoporosis
- Lower BMD longer the GCSF therapy- the pathology is not understood

Suggestions

- Screening Vitamin D levels and replacement if needed
- Routine weight and height measurements
- Dual x-ray absorptiometry (DXA) scan to evaluate bone health

Questions?